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08/246,034	05/18/94	PLATZ	R ITSY002000US

EXAMINER	
DEGEN, N	
ART UNIT	**PAPER NUMBER**
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DATE MAILED: 06/12/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 3/7/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1-17 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☑ Claims 1-17 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Part III DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior office action.

2. Claims 1-8 and 10-17 are rejected under 35 U.S.C. § 103 as being unpatentable over Platz et. al. (World Patent Application No. 91/16038) in view of Radhakrishnan (U. S. Patent No. 5,049,389).

Platz et. al. teaches that interferons may be aerosolized to a dry powder formation that contains human serum albumin and a carbohydrate as stabilizing/bulking agents, and has a particle size of between 0.5 to 10 microns (Platz, page 4, lines 15-28 through page 5, lines 1-2). Platz teaches that the particle size preferable for intrapulmonary administration is between 0.5-4 microns (Platz, page 7, lines 6-10). Platz teaches a specific dry powder composition that contains interferon-beta, human serum albumin, sodium chloride, and sorbitol (a carbohydrate bulking/stabilizing material) (Platz, page 9, lines 24-29). Platz teaches that the particle size of this composition is less than 4 microns (Platz, page 11, Table 2). Platz discloses that at least 75% of the particles are of a uniform size, which, in the case of the preferred embodiment may be construed as over 95% of the particles has a size of less than 10 microns. It may be construed that, since the composition contains only those

ingredients listed above, there are no penetration enhancers present in the composition. Platz teaches that this composition may be administered with a dry-powder inhaler to administer therapeutically meaningful dosages of interferon (Platz, page 9, lines 1-17).

Platz does not teach that the interferons may be made into a dry powder formulation by the technique of spray drying, nor that more than 80% of the particles have a size of less than 10 microns.

Radhakrishnan teaches that interferon may be encapsulated in liposomes, which, in turn, may be subjected to powder formation by either spray drying or lyophilization for use in inhalation therapy wherein the particle size of the powder formulation is 2.1 microns or less (Radhakrishnan, col. 14, lines 22-45 and col. 20, lines 25-68 through col. 21, lines 1-5). It would have been obvious to one with ordinary skill in the art at the time Applicants' invention was made to use either the spray drying technique of Radhakrishnan or the lyophilization and milling technique of Platz to form a dry powder composition of interferon because these are functionally equivalent processes, yielding a dry powder composition for intrapulmonary administration of interferon, and it is obvious to substitute one functional equivalent for another. Further, it would have been obvious to one with ordinary skill in the art at the time Applicants'

invention was made to make a powdered interferon preparation, such as the one suggested by Platz and Radhakrishnan, wherein more than 80% of the particles have a size of less than 10 microns because this smaller size will enable the interferon to be adsorbed through mucosal tissues at a much greater rate and such a preparation will therefore be able to deliver more active ingredients to a patient in need thereof in a shorter amount of time.

3. Claim 9 is rejected under 35 U.S.C. § 103 as being unpatentable over Platz et. al. (World Patent Application No. 91/16038) in view of Radhakrishnan (U. S. Patent No. 5,049,389) as applied to claims 1-8 and 11-17 above, and further in view of Patton et. al. (World Patent Application No. 93/00951).

Platz and Radhakrishnan suggest a method of preparing a spray dried interferon preparation as described above.

Neither of the abovementioned ~~authors~~ patentees teach that the dry powder interferon composition is aerosolized by the dispersement of a gas stream, nor that the aerosol is captured in a chamber with a mouthpiece.

Patton teaches an apparatus for the aerosolization of a dosage of a medicament for inhalation that comprises dispersion of a specific amount of the medicament in a volume of gas, wherein the medicament is in the form of a dry powder (Patton, page 4, lines 28-36). Patton also teaches that the aerosolized

dosage flows into a chamber and through a mouthpiece to the patient (Patton, page 4, lines 37-38 through page 5, line 1). It would have been obvious to one with ordinary skill in the art at the time Applicants' invention was made to use Patton's aerosolizer to aerosolize Platz's dry powder interferon formulation because this aerosolizer will effectively give a metered dose of interferon intrapulmonarily to any patient in an effective fashion, thereby enabling the patient to obtain needed treatment, resulting in better health.

Response to Amendment

4. The rejections made in the previous Office action have been withdrawn in favor of the new grounds of rejection set forth above.

5. Applicant's arguments filed March 7, 1995 have been fully considered but they are not deemed to be persuasive.

6. Applicants' argument that Platz does not anticipate the instant invention because Platz's interferons are not spray dried is deemed moot in light of the new grounds of rejection set forth above.

7. Applicants argue that Platz's interferon preparation contains a surfactant. However, the surfactant is only one embodiment of Platz's interferon composition, and a disclosed preferred embodiment does not teach away from non-preferred

embodiments. **In re Susi**, 169 USPQ 423 (CCPA 1971). Furthermore, Applicants' claims do not exclude the use of a surfactant.

8. Applicants argue that Radhakrishnan spray dries interferons in conjunction with liposomes, not interferon alone. However, the whole preparation of Radhakrishnan is being spray dried, which clearly means that the interferon itself is being spray dried. Further, there is no substantial loss of activity upon spray drying such interferon preparations. One of ordinary skill in the art at would therefore expect that a preparation of interferon not in conjunction with liposomes, which would be more desirable for a respirable preparation, would be able to undergo a spray drying procedure, also with no substantial loss of activity.

9. In response to Applicant's argument that there is no suggestion to combine the references, the Examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references. **In re Nomiya**, 184 USPQ 607 (CCPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. **In re McLaughlin**, 170 USPQ 209 (CCPA 1971). References are evaluated

by what they suggest to one versed in the art, rather than by their specific disclosures. **In re Bozek**, 163 USPQ 545 (CCPA) 1969. In this case, Applicants argue that, given Platz's dried interferon preparation, one would not look towards Patton for a method of aerosolization. However, since Platz does clearly teach that such a dried powder interferon preparation may be delivered via inhalation, one of ordinary skill in the art would be directed to look at all forms of delivery of such a preparation, of which aerosolization is one.

Conclusion

10. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Nancy J. Gromet-Degen, whose telephone number is (703) 308-3672. The Examiner can normally be reached on Monday-Thursday from 8:00 AM-5:30 PM. The Examiner can also be reached on alternate Fridays.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Michael G. Wityshyn, can be reached at (703) 308-4743. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703)308-0196.

MICHAEL G. WITYSHYN
SUPERVISORY PATENT EXAMINER
GROUP 1800

Nancy J. Gromet-Degen
June 6, 1995